engineering proceedings

Proceeding Paper

Towards Plasmonic Biosensors to Realize Point-Of-Care Tests for Viruses and Bacteria Detection †

Francesco Arcadio [1,*], Ines Tavoletta [2], Chiara Marzano [1], Luca Pasquale Renzullo [3], Nunzio Cennamo [1] and Luigi Zeni [1]

[1] Department of Engineering, University of Campania Luigi Vanvitelli, Via Roma 29, 81031 Aversa, Italy; chiara.marzano@studenti.unicampania.it (C.M.); nunzio.cennamo@unicampania.it (N.C.); luigi.zeni@unicampania.it (L.Z.)
[2] Department of Chemical Sciences, University of Naples Federico II, 80126 Naples, Italy; i.tavoletta@studenti.unina.it (I.T.)
[3] Department of Agricultural Sciences, University of Naples Federico II, 80055 Naples, Italy; lucpasrenz@gmail.com (L.P.R.)
* Correspondence: francesco.arcadio@unicampania.it; Tel.: +39-0815010367
† Presented at the 4th International Electronic Conference on Applied Sciences, 27 October–10 November 2023; Available online: https://asec2023.sciforum.net/.

Abstract: Optical fiber biosensors could be used to develop Point-Of-Care Tests (POCTs) for detecting viruses and bacteria in several matrices. In particular, the Surface Plasmon Resonance (SPR) and Localized SPR phenomena (LSPR) can be excited by exploiting low-cost and small-size optical fiber chips. Generally, SPR or LSPR sensors are realized using several kinds of modified optical fibers (silica, plastic, or specialty) or exploiting other optical waveguides (e.g., slab, spoon-shaped waveguides, etc.). More specifically, optical fiber sensors can be classified as intrinsic or extrinsic. In the "optical fiber intrinsic sensors", the sensing area is realized in the optical fiber directly, such as in the case of plasmonic platforms based on D-shaped plastic optical fibers (POFs), tapered optical fibers, U-bend POFs, or light-diffusing fibers (LDFs). On the opposite, when the optical fiber is used as a mere waveguide allowing the launch of light to the sensing region and its collection, it is defined as "optical fiber extrinsic sensors", like in the case of the plasmonic sensors realized by Cennamo et al. via POFs combined with spoon-shaped waveguides, 3D-printed platforms, bacterial cellulose waveguides, nano-gratings and InkJet printed based chips. To realize optical biosensor chips for viruses and bacteria detection, both intrinsic and extrinsic plasmonic POF sensors can be efficiently combined with receptors specific for membrane proteins, either biological (e.g., antibodies, aptamers, enzymes, etc.) or synthetic (e.g., molecularly imprinted polymers), to build groundbreaking POCTs.

Keywords: optical sensors; biosensor chips; Surface Plasmon Resonance (SPR); plastic optical fibers (POFs); Point-Of-Care Tests (POCTs)

Citation: Arcadio, F.; Tavoletta, I.; Marzano, C.; Renzullo, L.P.; Cennamo, N.; Zeni, L. Towards Plasmonic Biosensors to Realize Point-Of-Care Tests for Viruses and Bacteria Detection. *Eng. Proc.* **2023**, *52*, x. https://doi.org/10.3390/xxxxx

Academic Editor(s): Name

Published: date

1. Introduction

Immediately after the COVID-19 pandemic highlighted the need for small-size, inexpensive, and easy-to-use devices useful to detect the virus on site and with the capability of transmitting statistical data over the Internet, POCTs connected to the internet have gained large interest among the medical community [1]. In fact, during a pandemic emergency, these technologies can give a more accurate view of the state of emergency and improve and speed up its management.

Recently, optical biosensors based on Surface Plasmon Resonance (SPR) have been developed for several applications [2,3]. In particular, SPR probes and Molecularly Imprinted Polymer (MIP) receptors were successfully tested [4,5] for several bio/chemical applications, such as for SARS-CoV-2 detection in several matrices [6]. Thanks to the method's high sensitivity, the virus can be detected even in diluted samples. The proposed POCT for SARS-CoV-2 detection reported in [6] can detect the presence of the virus in a few minutes and transmit the outcome to a platform via the Internet, allowing automatic statistics useful for pandemic monitoring and management. Since this POCT also allows quantitative measures of the SARS-CoV-2, it can represent a valid tool for monitoring COVID-19 patients' treatment [6]. In particular, as shown in the outline of Figure 1, an SPR-POF probe [7], coupled with a specific MIP nanolayer [6], has been designed and tested for the recognition of SARS-CoV-2 via its spike protein with the possibility of transmitting the experimental data obtained in real-time [8].

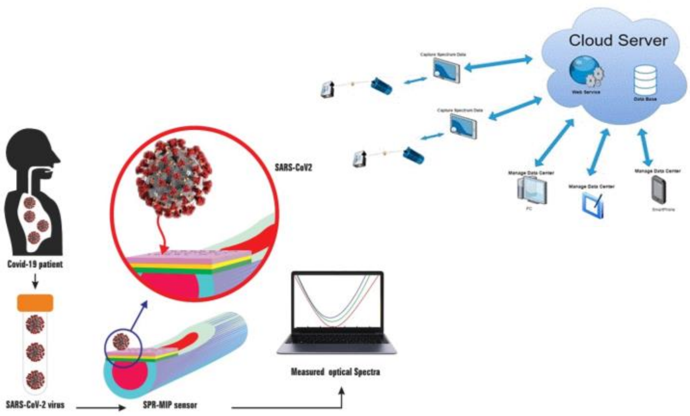


Figure 1. Scheme of the sensor to detect SARS-CoV-2 with the possibility of transmitting and storing the data in a cloud via the internet [6,8].

Concerning the molecular recognition element (MRE), it is important to mention the possibility of using several specific MIPs (imprinted for different substances) in order to realize a versatile sensor system based on the same optical platform covered with a "programmable" MIP layer, as outlined in Figure 2. So, the potential of the proposed POCT is that it can be quickly updated/developed for a new pandemic emergency or different types of pathogens or viruses of interest. The reprogramming of the MIP is possible because the synthesis process involves a copolymerization between appropriate functional monomers and a crosslinking agent in the presence of the target molecule [4,5,9–11].

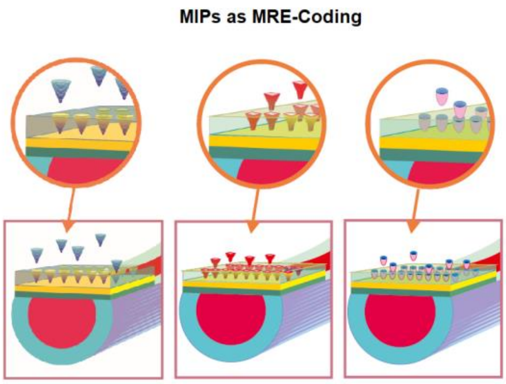
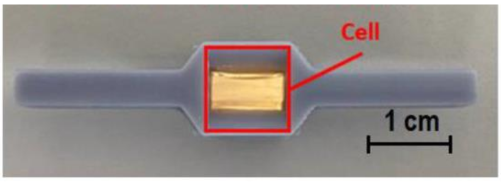


Figure 2. Outline of a SPR-POF platform combined with several MIP layers [6].

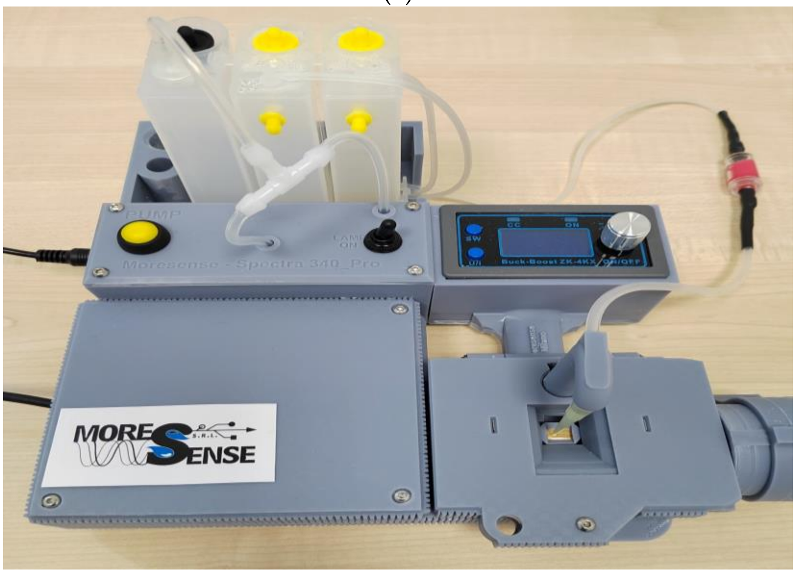
This work reports a mini-review of the capabilities of the POF sensors for viruses and bacteria detection via POCT.

2. POCT: SPR-POF-MIP Chips and Experimental Setups

The plasmonic POF-based sensor platforms and the setup used to carry out this POCT were manufactured by Moresense srl (Spectra 340, Moresense srl, Milan, Italy). Figure 3a shows an image of the SPR-POF probe covered by the specific MIP layer, whereas the POCT is reported in Figure 3b. A developed software tool (Moresense Capture Spectrum Data ver. 2.3) is used to acquire and process the experimental data of the POCT. This tool offers the possibility to connect the POCT to the internet.



(**a**)



(**b**)

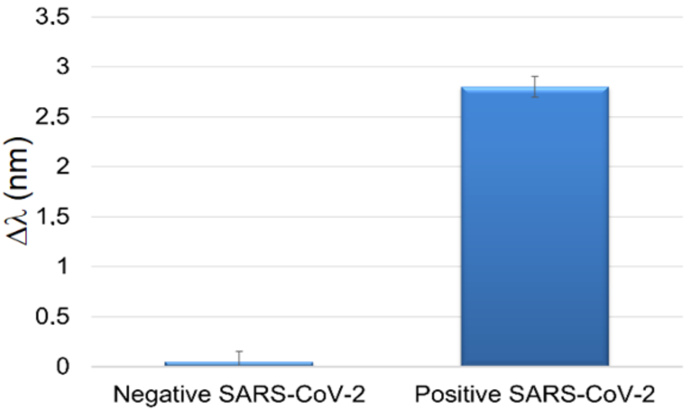
Figure 3. Pictures of the (**a**) SPR-POF-MIP chip and POCT (**b**), both manufactured by Moresense srl (Milan, Italy) in collaboration with the University of Campania Luigi Vanvitelly (Naples, Italy).

3. How to Measure the SARS-CoV-2 Detection in UTM

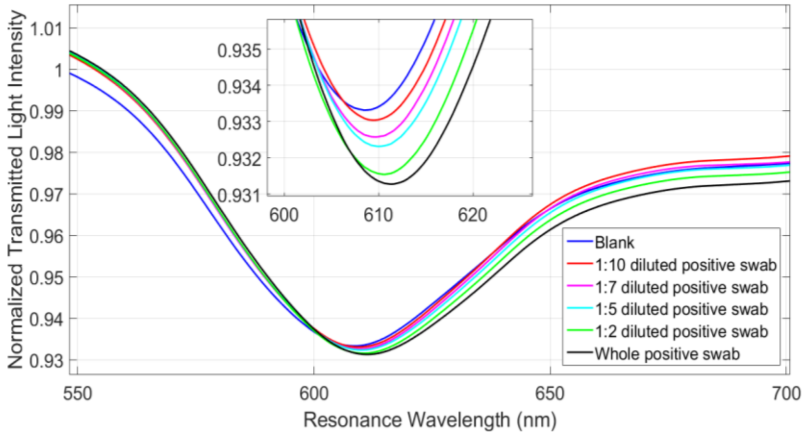
An analysis for detecting the SARS-CoV-2 Spike S1 protein and the SARS-CoV-2 virus has been reported in [6,8] and here recalled to demonstrate the capabilities of the POF-based bio/chemical sensors and the proposed sensing approach.

Positive and negative nasopharyngeal (NP) swabs for COVID-19 were collected to carry out these measurements [6,8]. In particular, the previously positive samples were analyzed with the proposed POCT and in parallel with the RT-PCR technique (gold standard).

Figure 4a reports the experimental results obtained by the SPR-POF-MIP sensor with real SARS-CoV-2 positive and negative samples of nasopharyngeal (NP) swabs in UTM (universal transport medium) [6]. Each experimental data is the result of an average of five successive acquisitions, and the error bar shows the standard deviation. Figure 4b shows the SPR spectra of a positive NP swab in UTM diluted with a physiological solution at different dilution factors [6]. In this way, it was possible to show that SARS-CoV-2 quantitative measurements can be carried out. Using the UTM as a means, shifts in the resonance wavelength were found for dilutions minor than 1:10. The same samples were tested using RT-PCR and were positive only when diluted 1:2 (with a physiological solution).



(**a**)



(**b**)

Figure 4. (**a**) Comparison of the positive and negative responses in UTM obtained by the POCT (confirmed by RT-PCR). (**b**) SPR spectra at different dilutions of the positive sample in UTM (resulted positive for SARS-CoV-2 at the 36th RT-PCR cycle). Samples were diluted using the physiological solution.

4. Conclusions

The plasmonic POF-based POCT, aimed at detecting SARS-CoV-2, has proven to be highly sensitive in a real scenario. Its operation has proved effective in various real matrices, and the measurement system used is cheap, small dimensions, and connected to the internet.

Moreover, it should be specified that what is recalled here for detecting SARS-CoV-2 is only a proof of concept to demonstrate the efficiency of the presented POCT. However, it is possible to simply generalize this approach for other viruses or bacteria by reprogramming the MIP.

Author Contributions: Conceptualization, F.A., I.T., C.M., L.P.R., N.C. and L.Z.; methodology, F.A., I.T., C.M., L.P.R., N.C. and L.Z.; validation, F.A., I.T., C.M., L.P.R., N.C. and L.Z.; formal analysis, F.A., I.T., C.M., L.P.R., N.C. and L.Z.; investigation, F.A., I.T., C.M., L.P.R., N.C. and L.Z.; resources, N.C. and L.Z.; data curation, F.A., C.M., I.T., L.P.R., N.C. and L.Z.,; writing—original draft preparation, F.A., I.T., C.M., L.P.R., N.C. and L.Z.; writing—review and editing, F.A., I.T., C.M., L.P.R., N.C. and L.Z.; supervision, L.Z. and N.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data are available on reasonable request from the corresponding author.

Acknowledgments: The authors acknowledge the Regione Campania for the BETTER Project–POR. FESR CAMPANIA 2014-2020 program.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Guo, Y.R.; Cao, Q.D.; Hong, Z.S.; Tan, Y.Y.; Cheng, S.D.; Jin, H.J.; Tan, K.S.; Wang, D.Y.; Yan, Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak—An update on the status. *Mil. Med. Res.* **2020**, *7*, 11.
2. Nguyen, H.H.; Park, J.; Kang, S.; Kim, M. Surface Plasmon Resonance: A Versatile Technique for Biosensor Applications. *Sensors* **2015**, *15*, 10481–10510.
3. Gandhi, M.S.A.; Chu, S.; Senthilnathan, K.; Babu, P.R.; Nakkeeran, K.; Qia, L. Recent Advances in Plasmonic Sensor-Based Fiber Optic Probes for Biological Applications. *Appl. Sci.* **2019**, *9*, 949.
4. Gupta, B.; Shrivastav, A.; Usha, S. Surface Plasmon Resonance-Based Fiber Optic Sensors Utilizing Molecular Imprinting. *Sensors* **2016**, *16*, 1381.
5. Cennamo, N.; Pesavento, M.; Zeni, L. A review on simple and highly sensitive plastic optical fiber probes for bio-chemical sensing. *Sens. Actuators B Chem.* **2021**, *331*, 129393.
6. Cennamo, N.; D'Agostino, G.; Perri, C.; Arcadio, F.; Chiaretti, G.; Parisio, E.M.; Camarlinghi, G.; Vettori, C.; Di Marzo, F.; Cennamo, R.; et al. Proof of Concept for a Quick and Highly Sensitive On-Site Detection of SARS-CoV-2 by Plasmonic Optical Fibers and Molecularly Imprinted Polymers. *Sensors* **2021**, *21*, 1681.
7. Cennamo, N.; Massarotti, D.; Conte, L.; Zeni, L. Low cost sensors based on SPR in a plastic optical fiber for biosensor implementation. *Sensors* **2011**, *11*, 11752–11760.
8. Cennamo, N.; D'Agostino, G.; Pasquardini, L.; Arcadio, F.; Perri, C.; Coppola, N.; Angelillo, I.F.; Altucci, L.; Di Marzo, F.; Parisio, E.M.; et al.; Quantitative detection of SARS-CoV-2 virions in aqueous mediums by IoT optical fiber sensors. *Results Opt.* **2021**, *5*, 100177.
9. Haupt, K. Molecularly imprinted polymers in analytical chemistry. *Analyst* **2001**, *126*, 747–756.
10. Haupt, K.; Linares, A.V.; Bompart, M.; Bui, B.T.S. Molecularly Imprinted Polymers. *Top. Curr. Chem.* **2011**, *325*, 1–28.
11. BelBruno, J.J. Molecularly Imprinted Polymers. *Chem. Rev.* **2019**, *119*, 94–119.